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Alteration of Cardiovascular Autonomic Functions by Vegetarian Diets in Postmenopausal Women Is Related to LDL Cholesterol Levels

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Abstract

This study was designed to test the hypothesis that alteration of cardiovascular autonomic functions by vegetarian diets in healthy postmenopausal women is related to lipid metabolism. A total of 70 healthy postmenopausal women not on hormone therapy participated in this study: 35 were vegetarians (mean age 55.0 years) and 35 were omnivores (mean age 55.1 years). Cardiovascular autonomic functions and baroreflex sensitivity were evaluated by specific frequency-domain measures of heart rate variability (HRV) and arterial blood pressure fluctuation. The vegetarians had statistically significant lowered blood pressure, total cholesterol, low-density lipoprotein (LDL) cholesterol, triglyceride, and fasting glucose levels compared with the omnivores. The vegetarians exhibited a significant higher total power, low-frequency (LF; 0.04-0.15 Hz) and high-frequency (HF; 0.15-0.4 Hz) of HRV and increased baroreflex sensitivity measures [Brr(LF) and Brr(HF)] compared with the omnivores. Total power, LF and HF of HRV, Brr(LF), and Brr(HF) were significantly and negatively correlated with LDL-cholesterol concentrations ($P < 0.01$). We concluded that the increases of cardiac vagal activity and baroreflex sensitivity by vegetarian diets in postmenopausal women are inversely related to LDL-cholesterol levels.

Key Words: vegetarian diets, postmenopausal women, low-density lipoprotein, coronary artery disease, heart rate variability, frequency-domain analysis

Introduction

Epidemiological studies have revealed that the incidence of cardiovascular disease is higher in postmenopausal women than in age-matched men and premenopausal women (12, 17) because of higher arterial blood pressure (ABP), dyslipidemia (19), insulin resistance (3) and atherosclerotic progression (20). Although a deficiency of estrogen is a major cause, it remains less clearly demonstrated whether other physiological factors are involved.

Postmenopausal women have been shown to have disturbed activity of cardiac autonomic functions (1). One study showed that cardiac vagal activity is related to the risk or severity of cardiovascular disease or sudden cardiac death (22). Epidemiological

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evidence also shows depressed baroreflex sensitivity is associated with reduced survival secondary to coronary artery disease (CAD) (9). Therefore, alteration of cardiac autonomic functions might be a contributing factor for the increased incidence of CAD in women after menopause.

Our previous study showed that postmenopausal women eating a vegetarian diet had an increase in cardiac vagal functions and baroreflex sensitivity, as well as optimal lipid profiles and blood pressure (8); this was determined with frequency-domain analysis of heart rate variability (HRV). To determine whether the vagotonic effect of vegetarian diets in postmenopausal women is related to the decreased lipid concentrations, we designed this study to test the hypothesis that alteration of cardiovascular autonomic functions by vegetarian diets in healthy postmenopausal women is related to lipid metabolism.

Materials and Methods

Study Sample and Experimental Setup

The participants were recruited from the health check-up department of Tzu Chi Dalin General Hospital. A total of 70 healthy postmenopausal women not taking hormone replacement therapy were recruited into this study. Thirty-five vegetarians, who had been vegetarian by themselves for 2 to 35 years (mean duration 7.9 years) ate no meat or fish because of their religious belief, but some occasionally consumed eggs and milk (ovo-lactovegetarians) in small amounts. The control group comprised 35 age-matched healthy omnivores. A detailed questionnaire was administered and a complete medical history was taken from each subject. Physical and neurological examinations were conducted for each patient. Subjects with systemic diseases or arrhythmia were excluded. Complete blood count, serum lipid profile, fasting blood sugar, and uric acid concentrations were determined to exclude those patients with diabetes mellitus, thyroid disease or infectious diseases. Furthermore, no subjects smoke cigarettes, drank alcoholic beverages or took any medications reported to influence cardiovascular functions. The procedures used in this study were approved by the Human Research Committee of Tzu Chi Dalin General Hospital, and all subjects were given with informed consent.

Recording of ABP and ECG

Instantaneous ABP and electrocardiogram (ECG) recordings were taken for 5 min in the daytime while each subject sat quietly and breathed normally. ABP was recorded non-invasively using a continuous blood pressure monitor (CBM-700, Colin, Komaki City, Aichi, Japan). ECG recordings were obtained by precordial leads. ABP and ECG signals were recorded using a 12-bit analog-to-digital converter (PCL-818, Advantech, Hualien, Taiwan, R.O.C.) with a sampling rate of 1024 Hz. All biological signals were acquired, displayed, and stored on a personal computer (IBM-PC compatible) for off-line verification.

Auto-Spectral Analysis of ABP and HRV

The analysis technique for ABP and ECG variations was previously documented (25). The original ABP signals were subject to off-line spectral analysis by the construction of an average periodogram. For this purpose, a 288-s segment of stable ABP signals was divided into 8 sets of 64-s windows. Each set overlapped the next set by 50%. Computation of the spectrum was performed using fast Fourier transform. The ABP spectra obtained for the 8 data sets were subsequently averaged to minimize contributions from variable noise and to sharpen reproducible spectral components. The computer program subsequently quantified each spectral component by method of integration. We focused on the lower end of the frequency, including very-low-frequency (0.016-0.04 Hz), low-frequency (LF, 0.04-0.15 Hz) and high-frequency (HF, 0.15-0.4 Hz).

Processing of ECG signals for HRV was performed with a standard procedure[1]. Each QRS complex was identified. The R point of each valid QRS complex was defined as the time point of each heart beat, and the interval between two R points (R-R interval) was estimated as the interval between the current and latter R points (interpulse interval). Frequency-domain analysis of HRV was also performed using the nonparametric method of Fourier transform. For each time segment (288 s, 2048 data points), our algorithm estimated the power spectral density on the basis of Fourier transform. The resulting spectrum was corrected for attenuation resulting from the sampling and the Hamming window. The power spectrum was subsequently quantified into various frequency-domain indices as total power, LF (0.04-0.15 Hz) and HF (0.15-0.40 Hz) power, LF in normalized units (LF%), and ratio of LF to HF (LF/HF).

Cross-Spectral Analysis of ABP and HRV

Cross-spectral analysis of ABP and HRV signals

[1] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. *Circulation* 93: 1043-1065, 1996.

Table 1. Baseline characteristics of the 2 groups

	Omnivore (n = 35)	Vegetarian (n = 35)	P values
Age, y	55.1 ± 1.4	55.0 ± 1.3	0.965
Age of menopause, y	49.3 ± 0.7	49.4 ± 0.5	0.978
BMI, kg/m^2	23.8 ± 0.6	22.8 ± 0.5	0.168
SABP, mmHg	133.4 ± 2.6	121.1 ± 2.5	0.001
DABP, mmHg	81.7 ± 1.7	72.4 ± 2.0	0.001
HR, beats/min	77.0 ± 1.6	76.9 ± 1.8	0.989
Total cholesterol, mg/dl	203.6 ± 8.6	174.0 ± 4.3	0.004
LDL cholesterol, mg/dl	135.9 ± 6.8	111.6 ± 6.1	0.014
HDL cholesterol, mg/dl	49.4 ± 5.1	50.3 ± 6.2	0.874
Triglyceride, mg/dl	93.1 ± 8.4	63.1 ± 6.2	0.007
Fasting blood glucose, mg/dl	94.0 ± 1.7	87.8 ± 1.4	0.007
Uric acid, mg/dl	4.9 ± 0.2	4.4 ± 0.2	0.098

Values are presented as means ± SE; *n*: no. of subjects/group; BMI: body mass index; SABP: systolic arterial blood pressure; DABP: diastolic arterial blood pressure; HR: heart rate; LDL: low-density lipoprotein; HDL: high-density lipoprotein; *P* values: *vs*. omnivore by unpaired Student's *t*-test.

was conducted to evaluate the baroreflex sensitivity. A standard method in the evaluation of baroreflex sensitivity entailed measuring the slope of the regression line that relates reflex changes in heart rate in response to various degrees of transient hypertension. Because of the required systemic administration of vasopressors as phenylephrine, this method was deemed undesirable in our study. Instead, we evaluated spontaneous baroreflex sensitivity by using the recently established method. The magnitude of the ABP-HR transfer function was used. Coherence analysis indicates that fluctuations in ABP and HR were linearly correlated in the LF and HF ranges (7, 21). Thus the LF and HF magnitudes of the ABP-HR transfer function were used as the indicator for the spontaneous baroreflex sensitivity [Brr(LF) and Brr(HF)] (24).

Statistical Methods

All measured values are expressed as means ± standard error (SE). Natural logarithm transformation was applied to the spectral power of the ABP and HRV to adjust for the skewness of the distribution (16). Comparisons between 2 sets of data were performed with the unpaired Student's *t*-test. Pearson product-moment correlation coefficients were calculated to provide quantitative measures of the dependence between the total power, LF and HF of HRV, as well as baroreflex sensitivity measures [Brr(LF) and Brr(HF)] and age, body mass index (BMI), ABP, and total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, fasting glucose and uric acid concentrations. The statistical significance was set at $P < 0.05$ levels.

Results

Characterization and Cardiovascular Autonomic Measures

The mean ages, age of menopause and BMI between the omnivore and vegetarian groups did not significantly differ. The vegetarian group had significantly lower systolic and diastolic blood pressure, lowered serum's total cholesterol, LDL cholesterol, triglyceride, and fasting blood glucose concentrations than those of the omnivore group ($P < 0.05$) (Table 1). Quantitation of HRV indices and baroreflex sensitivity measures from the 2 groups showed that the vegetarian group had significantly higher total power, and LF and HF power of HRV compared with the omnivore group ($P < 0.05$). The vegetarian group exhibited a significant improvement in the Brr(LF) and Brr(HF) components compared with those of the omnivore group ($P < 0.05$) (Table 2). The above preliminary data have been published in 2006 (8).

Correlations

Table 3 shows the correlation between total power, LF and HF of HRV, and Brr(LF) and Brr(HF) with age, BMI, systolic ABP, diastolic ABP, and total cholesterol, LDL cholesterol, HDL cholesterol, fasting blood glucose and uric acid concentrations. Total power, LF and HF of HRV, Brr(LF) and Brr(HF) were significantly and negatively correlated with LDL cholesterol concentrations ($P < 0.01$). Total power and LF of HRV were significantly and negatively related with total cholesterol levels; HF of HRV and Brr(LF) were also

Table 2. Heart rate variability indices and baroreflex sensitivity measures of the 2 groups

	Omnivore (n = 35)	Vegetarian (n = 35)	P values
Heart rate variability indices			
Total power, ln(ms^2)	6.23 ± 0.17	6.90 ± 0.15	0.005
LF, ln(ms^2)	5.09 ± 0.21	5.75 ± 0.19	0.022
HF, ln(ms^2)	4.58 ± 0.14	5.28 ± 0.16	0.002
LF/HF, ratio	0.54 ± 1.4	0.51 ± 0.13	0.869
LF%, nu	51.87 ± 2.96	48.55 ± 3.17	0.448
Baroreflex sensitivity measures			
Brr(LF), ms/mmHg	2.87 ± 0.36	4.31 ± 0.41	0.011
Brr(HF), ms/mmHg	4.20 ± 0.40	5.99 ± 0.58	0.015

Values are presented as means ± SE; n: no. of subjects/group; LF: low-frequency power, HF: high-frequency power, LF/HF: ratio of LF to HF, and LF%: normalized LF in normalized units (nu) of heart rate variability; Brr(LF): low-frequency, and Brr(HF): high-frequency transfer magnitude between arterial blood pressure and heart rate variability; ln: natural logarithm; P values: *vs*. omnivore by unpaired Student's t-test.

Table 3. Correlation coefficients between heart rate variability variables (TP, LF and HF), and baroreflex sensitivity measures [(Brr(LF) and Brr(HF)], and age, BMI, blood pressure, lipid profiles, fasting glucose, and uric acid levels

	TP	LF	HF	Brr(LF)	Brr(HF)
Age	-0.124	-0.156	-0.095	-0.146	-0.395*
BMI	-0.199	-0.208	-0.128	-0.137	-0.024
SABP	-0.221	-0.124	-0.423*	-0.331†	-0.120
DABP	-0.225	-0.105	-0.230	-0.225	-0.124
Total cholesterol	-0.337†	-0.307†	-0.179	-0.230	-0.273
LDL cholesterol	-0.571*	-0.548*	-0.465*	-0.399*	-0.430*
HDL cholesterol	-0.231	-0.209	-0.160	-0.110	-0.064
Triglyceride	-0.333†	-0.233	-0.248	-0.279	-0.296
Fasting glucose	-0.170	-0.150	-0.070	0.119	0.137
Uric acid	-0.287	-0.238	-0.270	-0.043	-0.086

Pooled data n = 70; TP: total power; LF: low frequency power; HF: high frequency power; BMI: body mass index; SABP: systolic arterial blood pressure; DABP: diastolic arterial blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; $^*P < 0.01$; $^\dagger P < 0.05$.

significantly and negatively correlated with systolic ABP. A scatter plot of the correlation between LDL cholesterol concentrations and the total power of HRV, HF of HRV, Brr(LF) and Brr(HF) is given in Fig. 1.

Discussion

The major findings of this study are: [1] vegetarians of 2 or more years' duration have more favorable blood pressure measurements and lipid concentrations compared with omnivores; [2] vegetarian diets may increase the total power, LF and HF power of HRV and baroreflex sensitivity measures in healthy postmenopausal women; and [3] alteration of cardiovascular autonomic functions by vegetarian diets in healthy postmenopausal women is related to LDL cholesterol levels.

Frequency-domain analysis of HRV provides a unique aspect of autonomic regulation of the heart. Standards of measurement, physiological interpretations and clinical applications of HRV analyses have been well-documented since 1996[1]. The HF component of frequency-domain analysis of HRV is well-established to represent vagal regulation of the heart; LF% and LF/HF are considered to mirror sympathovagal balance or to reflect sympathetic modulations (16). In this

[1] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. *Circulation* 93: 1043-1065, 1996.

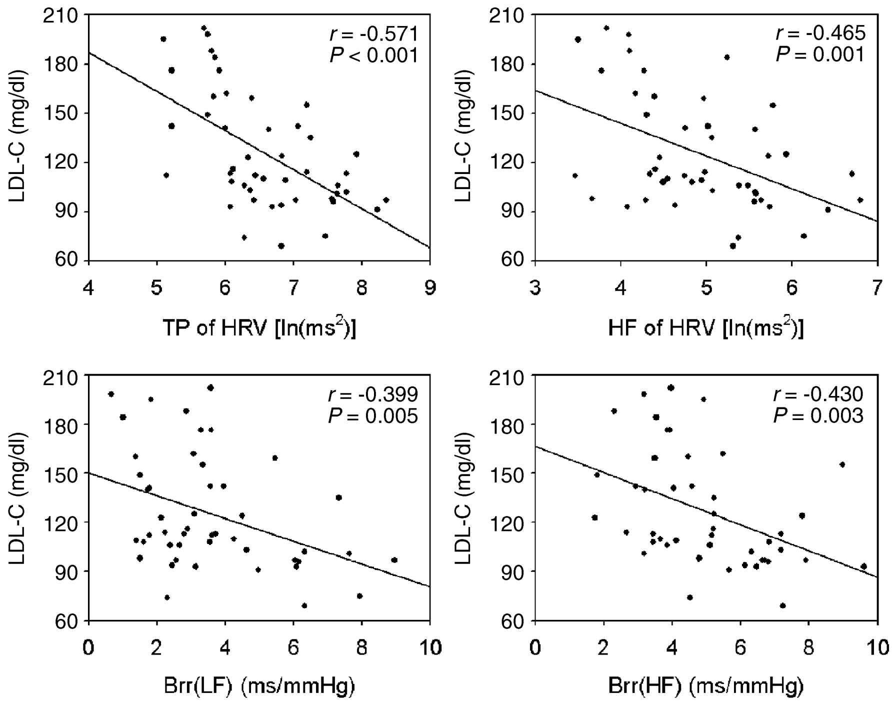

Fig. 1. Correlation between total power (TP) and high-frequency power (HF) of heart rate variability (HRV), as well as baroreflex sensitivity measures [Brr(LF) and Brr(HF)] and low-density lipoprotein cholesterol (LDL-C); ln: natural logarithm.

study, vegetarians had a higher HF power but similar LF% and LF/HF of HRV compared with the omnivores. These results suggest that vegetarian diets may facilitate vagal activities of the heart.

From cross-spectral analysis of ABP and HRV, we used the LF and HF transfer magnitude [Brr(LF) and Brr(HF)] as indicators for the baroreflex sensitivity (15). With this method, we also determined that Brr (LF) and Brr(HF)- levels significantly increased in the vegetarian group compared with the omnivore group, which demonstrated that long-term vegetarians had better baroreflex sensitivity.

Recent studies of vegetarians confirm a lower risk of fatal heart disease (13, 17, 23). The underlying mechanisms are multifactorial with some complex effects. It is well documented that a positive association exits between lipid levels and cardiovascular mortality[2]. Studies have also revealed that vegetarians have lower blood pressure measurements, and lower total and LDL cholesterol concentrations than do omnivores. These factors contribute to less progression of coronary atherosclerosis in vegetarians (17).

In this study, we found cardiovascular autonomic functions in postmenopausal women, including total power, LF and HF of HRV, Brr(LF), and Brr(HF) were all significantly and negatively related to serum LDL cholesterol concentrations. Hypercholesterolemia has been proved to be associated with a decreased 24-h HRV in men with and without CAD (5). Decreased HRV is a strong predictor of coronary mortality (10), so the fact that raised serum LDL cholesterol concentrations increase the mortality from CAD might partially be due to an impaired autonomic balance (5). Also treatment with the lipid-lowering agent, atorvastatin has been shown to increase in HRV level in hypercholesterolemic patients with or without CAD (18). In addition, serum LDL cholesterol is oxidized by macrophages to become oxidized LDL, which has important atherogenic properties by increasing inflammatory response (2). An increased inflammatory activity may also lead to poor prognosis in CAD by declining HRV levels (11).

In the Cholesterol and Recurrent Events (CARE) study (6), the magnitude of the endothelium-dependent vasodilatation was significantly correlated with the percentage change in LDL cholesterol concentration after administration of pravastatin. Therefore, the impaired endothelium-dependent arterial dilatation in the vessel walls caused by higher lipid levels might also change the baroreflex capacity (4, 5). That is consistent with our findings that baroreflex sensitivity is negatively correlated with LDL cholesterol levels. Accordingly, one of the underlying mechanisms linking vegetarian diets and cardiovascular autonomic

[2] National Cholesterol Education Program. Second report of the expert panel on detection, evaluation, and treatment of high cholesterol in adults (adult treatment panel II). *Circulation* 89: 1329-1445, 1994.

functions in postmenopausal women is associated with lower serum LDL cholesterol concentrations (14).

In fact, many factors, such as lifestyle and physical exercises may influence the physiological measurements. In this study, we have attempted to adjust for these factors during the subject selection process. The recruited subjects were nonsmokers, did not consume alcoholic beverages, did not receive hormone therapy for their postmenopausal status, were non-athletes, had a similar age of menopausal onset, had equal BMI, and were generally healthy. These parameters were considered sufficient to reduce the possibility of confounding the date and to increase the validity of the results. However, the presence of cardiac arrhythmia is a limitation of this study, which may make frequency-domain analysis of cardiovascular measures hard to be interpreted.

Our study results, although only a small, cross-sectional observation, conclude that in postmenopausal women, long-term vegetarians have lower blood pressure measurements and lipid concentrations compared with the omnivores. Vegetarian diets also facilitate vagal regulation of the heart and increase baroreflex sensitivity. Furthermore, the increases of cardiac vagal activity and baroreflex sensitivity in postmenopausal women are related inversely to LDL cholesterol levels.

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References

1. Banach, T., Dobrek, L., Milewicz, T., Kolasinska-Kloch, K., Krezysiek, J. and Thor, P.J. Effect of hormonal replacement therapy on autonomic regulation of the heart. *Przegl. Lek*. 61: 509-513, 2004.
2. Berliner, J.A. and Heinecke, J.W. The role of oxidized lipoproteins in atherogenesis. *Free Radic. Biol. Med*. 20: 707-727, 1996.
3. Carr, M.C. The emergence of the metabolic syndrome with menopause. *J. Clin. Endocrinol. Metab*. 88: 2404-2411, 2003.
4. Chowienczyk, P.J., Watts, G.F., Cockcroft, J.R. and Ritter, J.M. Impaired endothelium-dependent vasodilatation of forearm resistance vessels in hypercholesterolemia. *Lancet* 340: 1430-1432, 1992.
5. Christensen, J.H., Toft, E., Christensen, M.S. and Schmidt, E.B. Heart rate variability and plasma lipids in men with and without ischemic heart disease. *Atherosclerosis* 145: 181-186, 1999.
6. Cohen, J.D., Drury, J.H., Ostdiek, J., Finn, J., Babu, B.R., Flaker, G., Belew, K., Donohue, T. and Labovitz, A. Benefits of lipid lowering on vascular reactivity in patients with coronary artery disease and average cholesterol levels: a mechanism for reducing clinical events? *Am. Heart J*. 139: 734-738, 2000.
7. De Boer, R.W., Karemaker, J.M. and Strackee, J. Hemodynamic fluctuations and baroreflex sensitivity in humans: a beat-to-beat model. *Am. J. Physiol*. 253: H680-H689, 1987.
8. Fu, C.H., Yang, C.C.H., Lin, C.L. and Kuo, T.B.J. Effects of long-term vegetarian diets on cardiovascular autonomic functions in healthy postmenopausal women. *Am. J. Cardiol*. 97: 380-383, 2006.
9. Gmitrov, J. and Andrejko, S. Effect of verapamil on baroreflex sensitivity and on cardiovascular variability. *Wien. Klin. Wochenschr*. 112: 162-168, 2000.
10. Hartikainen, J.K., Malik, M., Staunton, A., Poloniecki, J. and Camm, J. Distinction between arrhythmic and non-arrhythmic death after myocardial infarction based on heart rate variability, signal-averaged electrocardiogram, ventricular arrhythmias and left ventricular ejection fraction. *J. Am. Coll. Cardiol*. 28: 296-304, 1996.
11. Janszky, I., Ericson, M., Lekander, M., Blom, M., Buhlin, K., Georgiades, A. and Ahnve, S. Inflammatory markers and heart rate variability in women with coronary disease. *J. Intern. Med*. 256: 421-428, 2004.
12. Kannel, W.B., Hjortkand, M.C., McNamara, P.M. and Gordon, T. Menopause and risk of cardiovascular disease: the Framingham study. *Ann. Intern. Med*. 85: 447-452, 1976.
13. Key, T.J., Thorogood, M., Appleby, P.N. and Burr, M.L. Dietary habits and mortality in 11000 vegetarians and health conscious people: results of a 17 year follow up. *Brit. Med. J*. 313: 775-779, 1996.
14. Kimura, T., Matsumoto, T., Akiyoshi, M., Owa, Y., Miyasaka, N., Aso, T. and Moritani, T. Body fat and blood lipids in postmenopausal women are related to resting autonomic nervous system activity. *Eur. J. Appl. Physiol*. 97: 542-547, 2006.
15. Kuo, T.B.J., Yien, H.W., Hseu, S.S., Yang, C.C.H., Lin, Y.Y., Lee, L.C. and Chan, S.H.H. Diminished vasomotor component of systemic arterial pressure signals and baroreflex in brain death. *Am. J. Physiol*. 273: H1291-H1298, 1997.
16. Kuo, T.B.J., Lin, T., Yang, C.C.H., Li, C.L., Chen, C.F. and Chou, P. Effect of aging on gender differences in neural control of heart rate. *Am. J. Physiol*. 277: H2233-H2239, 1999.
17. Mozaffarian, D., Rimm, E.B. and Herrington, D.M. Dietary fats, carbohydrate, and progression of coronary atherosclerosis in postmenopausal women. *Am. J. Clin. Nutr*. 80: 1175-1184, 2004.
18. Pehlivanidis, A.N., Athyros, V.G., Demitriadis, D.S., Papageorgiou, A.A., Bouloukos, V.J. and Kontopoulos, A.G. Heart rate variability after long-term treatment with atorvastatin in hypercholesterolemic patients with or without coronary artery disease. *Atherosclerosis* 157: 463-469, 2001.
19. Poehlman, E.T., Toth, M.J., Ades, P.A. and Rosen, C.J. Menopause-associated changes in plasma lipids, insulin-like growth factor I and blood pressure: a longitudinal study. *Eur. J. Clin. Invest*. 27: 322-326, 1997.
20. Rackley, C.E. Hormones and coronary atherosclerosis in women. *Endocrine* 24: 245-250, 2004.
21. Robbe, H.W.J., Mulder, L.J.M., Ruddel, H., Langewitz, W.A., Veldman, J.B.P. and Mulder, G. Assessment of baroreceptor reflex sensitivity by means of spectral analysis. *Hypertension* 10: 538-543, 1987.
22. Singh, J.P., Larson, M.G., Tsuji, H., Evans, J.C., O'Donnell, V.C.J. and Levy, D. Reduced heart rate variability and new-onset hypertension: insights into pathogenesis of hypertension: the Fragmingham Heart Study. *Hypertension* 32: 293-297, 1998.
23. Szeto, Y.T., Kwok, T.C. and Benzie, I.F. Effects of a long-term vegetarian diet on biomarkers of antioxidant status and cardiovascular disease risk. *Nutrition* 20: 863-866, 2004.
24. Yang, C.C.H., Kuo, T.B.J. and Chen, S.H.H. Auto-and cross-spectral analysis of cardiovascular fluctuations during pentobarbital anesthesia in the rat. *Am. J. Physiol*. 270: H575-H582, 1996.
25. Yien, H.W., Hseu, S.S., Lee, L.C., Kuo, T.B.J., Lee, T.Y. and Chan, C.C.H. Spectral analysis of systemic arterial pressure and heart rate signals as a prognostic tool for the prediction of patient outcome in intensive care unit. *Crit. Care Med*. 25: 258-266, 1997.